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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,686	03/30/2004	M. Youssouf Badal	134.02US	8305

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EXAMINER	
TIDWELL, JUDY LILLE	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/814,686	BADAL ET AL.	
	Examiner	Art Unit	
	Judy Lille Tidwell, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *6-8,10,13-15,17-20 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9,11,12,16,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-6, 8-16, 21-22, including the elected species "fixed tissue sample" and "colorectal cancer" in the reply filed on 4/26/2006 is acknowledged. Claims 6-8, 10, 13-15, 17-20, 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-5, 9, 11-12, 16, 21-22 are under consideration and examined on the merits.

Information Disclosure Statement

The Information Disclosure Statements filed on 6/23/2004 and 8/29/2004 has been considered. A signed copy of the 1449 form is attached hereto.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the preamble says the claimed invention is a method to determine a status of cancer. However, the active step does not have any step about how the purpose set out in the preamble is accomplished.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 9, 11, 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Tabiti et al. (US 5,888,746 issued 3/30/1999).

Claim 1 is drawn to a method of determining disease status of a patient suffering from a disease characterized by aberrant expression of one or more intracellular complexes, comprising measuring directly in a patient sample an amount of the intracellular complex, comparing said amount to its corresponding reference sample, and correlating differences from the patient sample and the reference sample to the disease status of the patient. Claim 2 further limits the base claim wherein the patient sample is a fixed tissue sample. Claims 5, 9, 11 further limit the base claim wherein the disease is a cancer. Claim 12 further limits the cancer to be colorectal cancer.

Tabiti et al. teach a method for diagnosis or prognosis of a cancer, comprising detecting an intracellular complex, protein tyrosine phosphate alpha (PTPα), in a sample from a subject, comparing the level in the first sample with the level in a second sample from normal tissue, wherein the cancer is colorectal cancer and wherein any overexpression is indicative that the first sample is from a cancerous tissue (column 10, claims 1-7). Tabiti et al. teach that protein tyrosine phosphatases are intracellular complexes in that they consist of non-receptor and receptor-like enzymes (column 1, lines 52-55). The level of PTPα expression is increased in tumors, therefore Tabiti et al. teach using PTPα as an intracellular marker for the diagnosis and prognosis of cancer (column 2, lines 47-50). Tabiti et al. disclose a method of comparing the level of PTPα in a first biological sample derived from tissue suspected of being neoplastic and comparing it to the level in a second, or control, biological sample derived from normal tissue (column 2, lines 53-57). Tabiti et al. determine the level of PTPα in tissue samples prepared by conventional histopathological techniques (column 4, line 1), such as fixed tissue samples fixed with fresh picric acid paraformaldehyde (column 7, lines 52-60). Furthermore, clinical data from patients with Duke's D stage tumors, a type of colon cancer, were examined for PTPα and the results were then correlated to their disease status (column 9).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3, 4, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tabiti et al. (US 5,888,746 issued 3/30/1999) in view of Masters and Fu (Journal of Biological Chemistry, 2001).

Claims 3, 4, and 21 are drawn to a method of determining the disease status of a cancer patient by measuring the intracellular complex 14-3-3//BAD.

Tabiti et al. teach as set forth above but do not teach measuring the intracellular complex 14-3-3//BAD.

Masters and Fu teach that 14-3-3 binds to and inhibitis the pro-apoptotic protein BAD and that 14-3-3 through binding to BAD and other ligands is critical for cell survival signaling (abstract). Additionally, Masters and Fu teach that difopein disrupts the 14-3-3//BAD complex and may liberate free active BAD (page 45199, right column). Therefore, inhibition of 14-3-3, namely with difopein, may represent a useful therapeutic

target for treatment of cancer and other diseases involving inappropriate cell survival (abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute measuring the intracellular complex, PTPα, in a patient sample for diagnosis or prognosis of cancer in order to determine the disease status as taught by the method of Tabiti et al. with the 14-3-3//BAD complex of Masters and Fu because Tabiti et al. teach comparing the level of the intracellular complex in the first sample with the level in a second sample from normal tissue, wherein any aberrant expression is indicative that the first sample may be from a cancerous tissue and overexpression of 14-3-3 in a cancerous cell may be inhibiting the normal function of BAD and other pro-apoptotic proteins. Based on the teachings of Tabiti et al. and Masters and Fu, one of ordinary skill in the art would have arrived at the claimed invention with a reasonable expectation of success. Furthermore, one would have been motivated to practice the claimed invention because the identification of intracellular complexes that are abnormally present in cancerous cells or tissues may represent useful targets for cancer treatment.

Claims 16 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tabiti et al. (US 5,888,746 issued 3/30/1999) and Masters and Fu (Journal of Biological Chemistry, 2001) as applied to claims 1-5, 9, 11-12, 21 above, and further in view of Singh et al. (US 6,627,400, issued 9/30/2003, filed 10/27/2000, IDS item).

Claims 16 and 22 are drawn to a method of determining disease status of a patient suffering from a disease characterized by aberrant expression of one or more intracellular complexes, comprising measuring directly in a patient sample an amount of the intracellular complex, comparing said amount to its corresponding reference sample, and correlating differences from the patient sample and the reference sample to the disease status of the patient, wherein the intracellular complex is determined by providing a cleaving probe having a cleavage-inducing moiety and a binding compound each having a molecular tag attached by a cleavable linkage, mixing the cleaving probe with said patient sample such that the cleaving probe binds to the targeted intracellular

complex and the cleavable linkage is within the effective proximity so that the molecular tag is released, and separating and identifying the released molecular tags to determine the presence or absence of the intracellular complex. Claim 16 ~~is drawn to~~ depends on claim 1-5, 11-12 and claim 22 ~~is drawn to~~ depends on claim 21. mg 7-9-06

Tabiti et al. and Masters and Fu teach as set forth above but do not teach the method steps of claims 16 and 22.

Singh et al. teach a method for determining cellular expressions (column 1, lines 19-24), more specifically populations of surface membrane proteins in a cell sample comprising mixing the membrane proteins with binding compounds having releasable eTag reporters attached thereto by a cleavable linkage and binding compounds conjugated with an active species producing moiety, whereupon the active species causes the cleavage of the eTag reporters when the binding compounds having the releasable eTag reporter is complexed with the conjugated binding compound and the eTag reporter is separated and identified, resulting in the determination of the amount of surface membrane protein in a cell sample (claim 12).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to apply the method of Singh et al. for determining the population of surface membrane proteins to the method of Tabiti et al for measuring the intracellular complex, PTPα, in a patient sample for diagnosis or prognosis of cancer in order to determine the disease status in combination with the 14-3-3//BAD complex of Masters and Fu because Singh et al. teach a powerful tool for detecting surface membrane proteins and determining changes in the surface protein population due to neoplasia (column 86, lines 27-34). Based on the teachings of Tabiti et al., Masters and Fu, and Singh et al., one of ordinary skill in the art would have arrived at the claimed invention with a reasonable expectation of success. Furthermore, one would have been motivated to practice the claimed invention because the identification of intracellular complexes that are abnormally present in cancerous cells or tissues may represent useful targets for cancer treatment.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Judy Lille Tidwell, PhD whose telephone number is 571-272-5952. The examiner can normally be reached on 8:00AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JLT
Art Unit 1642

MISOOK YU
PRIMARY EXAMINER